

	PDB code	SEQUENCE NATIVE	SELECTED RESIDUE	RMSD RANK1	RANK1/NATIVE SEQUENCE ALIGNMENT	RMSD BEST TOP10	BEST TOP10/NATIVE SEQUENCE ALIGNMENT	RANK1 CONTACTS / NATIVE CONTACTS (RESIDUES)
1	<b>1ELW</b>	GPTIEEVD	77	3.2	TFVHG--- GPTIEEVD	3.2	TFVHG--- GPTIEEVD	7/15
2	<b>1H6W</b>	SLNYIIKVKE	104	0.4	---FIIA--- SLNYIIKVKE	0.4	---FIIA--- SLNYIIKVKE	18/26
3	<b>1N7F</b>	ATVRTYSC	19	0.9	---GEYKI ATVRTYSC	0.9	---GEYKI ATVRTYSC	12/14
4	<b>1NVR</b>	ASVSA	74	2.7	-GTFCM ASVSA-	2.7	-GTFCM ASVSA-	7/7
5	<b>1TW6</b>	AVPI	54	0.9	ALKM AVPI	0.7	SRPE AVPI	8/8
6	<b>1UOP</b>	GFEP	595	3.5	PAVFKA --GFEP	3.5	PAVFKA --GFEP	11/13
7	<b>2B6N</b>	APT	222	3.9	GQPFGG --APT-	2.7	LLTP -APT	6/6
8	<b>2B9H</b>	RRNLKGLNLNLH	148	1.9	-----PVLVG- RRNLKGLNLNLH	1.8	-----PEPL--- RRNLKGLNLNLH	11/18
9	<b>2V3S</b>	GRFQV	21	-	GVIYG -	2.9	-RIQA GRFQV	9/11
10	<b>2XFX</b>	VGYPKVKEEML	155	3.8	---GHES---- VGYPKVKEEML	3.6	---GHVK---- VGYPKVKEEML	9/31
11	<b>3LNY</b>	EQVSAV	22	1.6	-PEAVV EQVSAV	0.7	PQVTVV EQVSAV	14/14

12	<b>3MMG</b>	ETVRFQS	172	1.6	--MQLD ETVRFQS	0.9	GKVKAN- ETVRFQS	17/18
13	<b>3NJG</b>	PQIINRP	92	0.9	GRVFAY- PQIINRP	0.9	GRVFAY- PQIINRP	18/19
14	<b>3VQG</b>	VTLV	19	3.8	MCPV VTLV	0.9	DGADV -VTLV	9/10
15	<b>4DS1</b>	YAESGIQTDL	61	3.0	----AVSVT- YAESGIQTDL	1.0	--PAEVSG-- YAESGIQTDL	12/24
16	<b>4NNM</b>	YPTSI	25	1.2	PLEVSVV -YPTSI	1.2	PLEVSVV -YPTSI	16/16
17	<b>4Q6H</b>	VQDTRL	20	3.3	--DTQE VQDTRL	0.7	QLRITV VQDTRL	13/14
18	<b>4QBR</b>	ARTKQTA	74	0.6	PTKWTG- ARTKQTA	0.6	PTKWTG- ARTKQTA	13/16
19	<b>3NFK</b>	GETRL	19	1.2	-PTEV GETRL	1.2	-PTEV GETRL	12/13
20	<b>3BFW</b>	DSTITIRGYVR	13	3.0	-SYIKVIIG-- DSTITIRGYVR	3.0	-SYIKVIIG-- DSTITIRGYVR	23/32
21	<b>3GQ1</b>	WLF	22	1.1	QKPR -WLF	1.1	QKPR -WLF	10/13
22	<b>2OY2</b>	IAG	75	-	KTIC -	3.1	GTVVVG ---IAG	8/9
23	<b>3BS4</b>	NIF	181	-	QDEQG -	-	-	4/19
24	<b>2OXW</b>	IAG	76	1.1	GAKGVG -IAG--	1.1	GAKGVG -IAG--	9/9
25	<b>3CH8</b>	PQPVDSWV	30	3.0	----EVVL PQPVDSWV	0.9	----PDQV PQPVDSWV	17/21

26	<b>1NTV</b>	<u>NFDNPVYRKT</u>	136	2.7	SSLPSG---- NFDNPVYRKT	2.5	SSIAP---- NFDNPVYRKT	9/18
27	<b>3BRL</b>	ATSAKATQTD	83	-	TGGVG -	-	-	1/16
28	<b>1N12</b>	SDVAFRGNLLD	73	-	QTVG -	-	-	0/26
29	<b>3D1E</b>	GQLGLF	175	-	VIIG -	-	-	10/17
30	<b>3OBQ</b>	PTPSAPVPL	64	-	AIQG -	-	-	9/12
31	<b>2W0Z</b>	APPPRPPPKP	50	-	MIGG -	-	-	3/10
32	<b>2W10</b>	PPPRPTAPKPLL	51	-	VSTG -	-	-	4/13
33	<b>4V3I</b>	DLTRP	98	-	VLVL -	-	-	5/7
34	<b>1SVZ</b>	<u>PQFSLW</u>	164	-	TVRVVG -	-	-	0/18
35	<b>2QAB</b>	<u>KILHRLIQLD</u>	54	-	TIDAG -	-	-	7/11
36	<b>3IDG</b>	<u>ALDKWD</u>	94	-	PEIRK -	-	-	1/13
37	<b>3JZO</b>	<u>LTFEHYWAQLTS</u>	70	-	SVSVI -	-	-	11/15
38	<b>3UPV</b>	<u>PTVEEV</u> D	77	-	PDIG -	-	-	4/13
39	<b>4DGY</b>	<u>QLINTNGSWHIN</u>	108	-	WCMRN -	-	-	5/10

40	<b>4J8S</b>	<u>RRLPIFNRISVS</u>	25	-	SFVG -	-	-	8/14
41	<b>4N7H</b>	<u>EAPPSYAEV</u>	18	-	TVVGYVG -	-	-	2/10
42	<b>4WLB</b>	<u>SLLKKLLD</u>	69	-	ADVRPK -	-	-	11/15
43	<b>1OU8</b>	<u>GAANDENY</u>	49	-	AFVDG -	-	-	9/16
44	<b>2HPL</b>	<u>DDLYG</u>	27	-	PVGSV -	-	-	8/10
45	<b>2O02</b>	<u>GLLDALDLAS</u>	49	-	PVTL -	-	-	3/17
46	<b>3Q47</b>	<u>NPISDVED</u>	73	-	TMLL -	-	-	8/14
47	<b>4EIK</b>	<u>SLARRPLPPLP</u>	36	-	PTRTIG -	-	-	11/14
48	<b>3DS1</b>	<u>ITFEDLLDYYP</u>	64	-	LDVSA -	-	-	4/14
49	<b>3T6R</b>	<u>ARTKQ</u>	106	-	-	-	-	-
50	<b>4J44</b>	AIAV	57	-	-	-	-	-
51	<b>1B9J</b>	KLK	416	-	-	-	-	-
52	<b>4BTB</b>	PPPPPPPPP	196	-	-	-	-	-
53	<b>4C2C</b>	AVPA	72	-	-	-	-	-

Table S1 – The table reports the results of PepComposer on a benchmark of 53 protein – peptide complexes listed in (1). We report the PDB code of the complex structure, the sequence of the native peptide, and the residue selected as center for running PepComposer. The RMSD RANK1 column reports the RMSD between the designed and native peptide according to the alignment shown in the next column. When the best scoring peptide does not overlap with the native one, the column is empty. The same data are reported for the best fitting peptide among the top ten scoring ones (RMSD TOP10 and BEST TOP10/NATIVE SEQUENCE ALIGNMENT columns). In five cases (last rows) PepComposer does not find any backbone scaffold satisfying the parameters. The ratio shown in the last column is the number of the protein target residues contacted by the best scoring peptide that overlap with those contacted by the native one divided by the total number of the latter. Underlined native sequences indicate cases where the native peptide is in a secondary structure element. As described in the main text, only backbone scaffolds showing an extended conformation are selected for the design.

1. Hauser, A.S. and Windshugel, B. (2016) LEADS-PEP: A Benchmark Data Set for Assessment of Peptide Docking Performance. *J Chem Inf Model*, **56**, 188-200.